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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/582,808
Filing Date: October 16, 2000
Appellant(s): MENDEL-HARTVIG ET AL.

Holly D. Kozlowski
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed December 27, 2005.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The following are the related appeals, interferences, and judicial proceedings known to the examiner which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

The Board may consider the copending appeal in Application 09/582,734

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

5,989,921	CHARLTON et al.	11-1999
4,415,700	BATZ et al.	11-1983

5,149,622	BROWN et al.	09-1992
3,720,760	BENNICH et al.	03-1973
5,846,703	DEVLIN et al.	12-1998
4,981,786	DAFFORN et al.	01-1991
4,446,231	SELF	05-1984

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 42, 43, 47, 51-53, 56-57, 59-61, 63, 64, 68, 72-74, 77-78 and 80-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Charlton et al (US 5,989,921) in view of Batz et al (US 4,415,700) and Brown et al (US 5,149,622).

Charlton et al disclose an immunoassay method for determining the presence of a ligand (analyte) in a sample. Charlton et al disclose applying a sample to an inlet of a test device which comprises a sorbent material which defines a lateral flow path, capable of transporting an aqueous solution by capillary action to a test site (detection zone). Charlton et al disclose that a conjugate comprising a protein bound to a colored particle (Reactant*) is mixed with the sample and inserted into the test device. Charlton et al also disclose that the conjugate may be predeposited in the test strip upstream of the test site (detection zone). Charlton et al disclose that the conjugate and sample flows to the test site (detection zone), which comprises latex particles entrapped or fixed in the flow path having an immobilized protein (antibody)(capturer) on their surface. Charlton et al disclose that if the analyte is present it reacts with immobilized binding protein (antibody) at the test site and forms a sandwich comprising immobilized binding protein-ligand binding protein colored particle (Reactant*) (col 3, line 21 – col 4, line 67). Charlton et al disclose that the color particles have a size of 18 nm (0.018 um) (col 8, lines 16-18). Charlton et al disclose that the beads trapped in the test site have a size

of 0.3 microns. Charlton et al also disclose packing the components into a test kit (col 4, line 17). Charlton et al disclose that the test cell can be used to detect any ligand (analyte) which has been assayed using known immunoassay procedures, or known to be detectable by such procedures (col. 4, lines 29-37).

Charlton et al differ from the instant invention in failing to teach the immobilized particles which exhibit hydrophilic groups on their surface. Charlton et al also fails to specifically teach the particles anchoring the capturer have a size, which is smaller than a smallest inner dimension of the flow channels of the matrix.

Batz et al disclose hydrophilic particles as carrier for biologically and /or immunologically active substances covalently bound to the particle (abstract). Batz et al disclose that the particles can carry substances such as, peptides, proteins, enzymes, hormones, vitamins, antigens, antibodies and micro-organisms (col 5). Batz et al disclose that the use of these hydrophilic particles provides for a diagnostic agent which has covalently bound biological and /or immunological active substances which do not impair the structure and thus the activity of the biologically active proteins (col 2, lines 59-68). Batz also disclose that these hydrophilic particles are especially useful for use in immunoassays (col 5, lines 16-19).

Brown et al disclose a flow device in which particles having a substance capable of reaction with the analyte in the sample, are immobilized in a matrix. Brown et al disclose that the average diameter of the particles is less than the average pore size of the matrix (see abstract). Brown et al disclose that by having the particle sizes having a size which is smaller than the flow channels of the matrix allows for an improved solid-

phase analytical device and a binding assay, which provides for a device which is relatively easy to use and require fewer procedural steps and less complex assay technique (col 4) and is highly advantageous over devices and assay methods of the prior art.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the hydrophilic particles as taught by Batz et al for the immobilized latex particles of Charlton et al because Batz et al teaches that these hydrophilic particles can be used as a solid phase in immunoassays and provides for a diagnostic agent which has covalently bound biological and /or immunological active substances which do not impair the structure and thus the activity of the biologically active proteins.

It also would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate particles which have a smaller diameter than that of the matrix as taught by Brown et al into the method of Charlton et al because Brown et al shows that by having the particle sizes having a size which is smaller than the flow channels of the matrix allows for an improved solid-phase analytical device and a binding assay which provides for a device which is relatively easy to use and require fewer procedural steps and less complex assay technique and is highly advantageous over devices and assay methods of the prior art.

Claims 44-46 and 65-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Charlton et al., Batz et al., and Brown et al in view of Bennich et al (US 3,720,760).

See above for teachings of Charlton et al., Batz et al., and Brown et al.

Charlton et al., Batz et al., and Brown et al. differ from the instant invention in failing to specifically teach a mixture of biospecific affinity reactants is immobilized to the hydropillic groups on the Capturer Particles.

Bennich et al disclose test allergens immobilized to particles. Bennich et al disclose that these allergens can be allergen extracts. Bennich et al disclose that the test allergen can be a mixture of two or more allergens which provides the advantage whereby a quick "yes" or "no" can be obtained during the examination to the question of whether hypersensitivity against one or more allergens in a large group of allergens is manifest.

It would have been obvious to one of ordinary skill in the art at the time the inventions was made to incorporate test allergens as taught by Bennich et al into the modified method of Charlton et al because Bennich et al shows that the test allergen can be a mixture of two or more allergens which provides the advantage whereby a quick "yes" or "no" can be obtained during the examination to the question of whether hypersensitivity against one or more allergens in a large group of allergens is manifest. Furthermore, Charlton et al disclose that the test cell can be used to detect any ligand which has been assayed using known immunoassay procedure, or known to be detectable by such procedures.

Claims 48, 50, 54, 55, 69, 71, 75 and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Charlton et al., Batz et al and Brown et al in view of Devlin et al (US 5,846,703).

See above for teachings of Charlton et al., Batz et al., and Brown et al.

Charlton et al., Batz et al, and Brown et al differ from the instant invention in failing to teach the analyte is an antibody of IgE type with specificity to allergens.

Devlin et al disclose that sandwich techniques can also be used to assay antibodies rather than antigens. Devlin et al also disclose determination of an antigen specific IgE by immobilizing antigens to solid phases. The antigens are biospecific for the corresponding antibody. Devlin et al disclose that these IgE antibodies are directed to an allergen (col 2, line 57 – col 3, line 1). Devlin et al disclose that this immunoassay allows for the measurement of antigenic substances in biological materials such as serum, plasma and whole blood and also allows for the determination of an allergen.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the use of immobilized antigens as taught by Devlin et al into the modified method of Charlton et al because Charlton et al disclose that that the test cell can be used to detect any ligand which has been assayed using known immunoassay procedures, or known to be detectable by such procedures and Devlin et al shows that this immunoassay allows for the detection of IgE and also allows for the measurement of antigenic substances in biological materials such as serum, plasma and whole blood and also allows for the determination of an allergen.

With respect to the flow channels having a smallest inner dimension and inner diameter and the particles anchoring the Capturer have a size in the range of 0.4-1000 um as recited in the instant claims, the optimum dimension and diameter of the flow channels and particle size can be determined by routine experimentation and thus would have been obvious to one of

ordinary skill in the art. Further, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980)

Claims 49, 58, 70 and 79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Charlton t al., Batz et al., and Brown et al ., in view of Dafforn et al (US 4,981,786).

See above for teachings of Charlton et al., Batz et al., and Brown et al.

Dafforn et al disclose the application of reagents upstream of a sample application site (col 13, lines 32-44) and also disclose detecting autoimmune antibodies (col 5, lines 1-8). Dafforn et al disclose that the application of reagents in this manner and the detection of autoimmune antibodies provides for a device which is simple, rapid, accurate, and safe and avoids contamination of various reagents during their addition to the device (col 2, lines 32-42) and provides for the detection of clinically important proteins (col 4, lines61-68).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the application of reagents and the detection of

autoimmune antibodies as taught by Dafforn et al into the modified method of Charlton et al because Dafforn et al shows that the application of reagents in this manner and the detection of autoimmune antibodies provides for a device which is simple, rapid, accurate, and safe and avoids contamination of various reagents during their addition to the device and provides for the detection of clinically important proteins.

Claims 62 and 83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Charlton et al, Batz et al and Brown et al in view of Self (US 4,446,231).

See above for teachings of Charlton et al, Batz et al and Brown et al. Charlton et al, Batz et al and Brown et al differ from the instant invention in failing to teach the diagnosis of an autoimmune disease.

Self discloses that immunoassays are used for the detection and/or determination of autoimmune diseases. Self et a disclose shows that immunoassays have a wide application, in both clinical and non-clinical fields and that they are particularly useful in any circumstance where it is necessary to detect and/or determine small or very small amounts of substances.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use immunoassays as taught by Self for the diagnosis of autoimmune diseases because Self et al show that immunoassays are used for the detection and/or determination of autoimmune diseases and that immunoassays have a wide application, in both clinical and non-clinical fields and that they are particularly useful in any circumstance where it is necessary to detect and/or determine small or very small amounts of substances. Furthermore, Charlton et al disclose that the test cell can be used to detect any ligand which

has been assayed using known immunoassay procedures, or known to be detectable by such procedures.

(10) Response to Argument

Appellant argues that the claims are nonobvious over the cited combination.

Appellant argues that Charlton et al does not teach or suggest a method or test kit as defined in claims 42 and 63 wherein a biospecific affinity reactant (Capturer) is firmly anchored to a flow matrix via immobilized particles exhibiting hydrophilic groups on their surface, particularly in combination with an analytically detectable reactant (Reactant*) having labeled particles as an analytically detectable group. Appellant argues that the hydrophobic particles of Charlton et al absorbed very strongly to flow matrices such as nitrocellulose membranes and that the hydrophobic features of the particles promote non-specific absorption of an analytically detectable reactant (Reactant*) and/or analyte and therefore decrease the specificity and accuracy of assays. Appellant argues that Charlton does not teach or suggest immobilized particles exhibiting hydrophilic groups on their surface. This is not found persuasive because the Examiner has not relied upon Charlton et al for teaching this limitation but rather has relied upon Batz et al for teaching the advantages of hydrophilic particles in binding assays and for their advantages over hydrophobic particles used in binding assays. Furthermore, Charlton et al disclose that any ligand, which has heretofore been assayed using known immunoassay procedures or known to be detectable by such procedures, can be used (col. 4).

Appellant argues that the deficiencies of Charlton et al are not resolved by Batz et al. Appellant argues that Batz et al does not teach or suggest a flow matrix immunoassay or use of the latex particles described therein in a flow matrix immunoassay. This is not found persuasive because Examiner has not relied upon the Batz et al reference for this limitation but rather has relied upon Charlton et al for teaching this limitation. Appellants state that there is no teaching or suggestion by Batz et al that their latex particles are suitable for adsorption to a second solid support or matrix. This is not found persuasive because although Batz et al does not specifically suggest that their latex particles are suitable for adsorption to a second solid support or matrix it is within the realm of one of ordinary skill in the art to replace one solid phase particle having immobilized biospecific affinity reactant for another solid phase particle comprising a biospecific affinity reactant because the use of solid phase particles in binding assays is very well known in the art. Further, Batz et al specifically teaches that these hydrophilic latex particles provides for a diagnostic agent which has covalently bound biological and/or immunological active substances and that immunologically active substances which are not bound covalently can be dissolved off during the measurement in the course of a diagnostic test. Therefore, Batz et al teaches the advantages of hydrophilic particles in diagnostic assays.

Appellant argues that Batz does not teach, suggest or recognize that their particles will provide improved sensitivity in flow matrices and decrease the tendency of non-specific absorption in a detection zone of a flow matrix as is obtained according to the present invention. This is not found persuasive because the fact that appellant has

recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Appellant states that in view of Batz et al's concern for impairment of reactant activity, one of ordinary skill in the art would be disinclined to absorb such particles to a second solid support, as one of ordinary skill in the art would presume that such adsorption would impair the structure and thus the activity of the biologically active proteins with which Batz et al are concerned. This is not found persuasive because as stated in the Advisory action this is not a concern, the Appellant has mischaracterized the Batz et al reference. Batz et al teaches that immunologically-active substances that are bound to the particles have not been impaired and are structurally active. Further, the statement made by Appellant concerning the impairment of reactant activity and structure by adsorption of the particle to a second solid support, is an assertion made by the Appellant without any support or evidence.

Appellant states that in the Advisory Action, the Examiner asserted that the concern regarding impairment of reactant activity is an assertion not support by the evidence. It appears that Appellant has misunderstood Examiner's statement. Examiner is stating that Appellant has not supplied any evidence that adsorption to a second solid support would impair the structure and the activity of the biologically active proteins. Examiner has relied upon Batz et al for teaching hydrophilic particles which have covalently bound immunologically-active substances and for teaching the

advantages of having these immunologically-active substances covalently bound to the hydrophilic particles. Therefore, the use of these hydrophilic particles is viewed as obvious and one of ordinary skill in the art would have a reasonable expectation of success substituting the hydrophilic particles of Batz et al. for the immobilized latex particles of Charlton et al.

Appellant argues that Brown et al fail to teach that the particle size is smaller than the flow channels of the matrix or, as required by the present claims, that the particles have a diameter smaller than a smallest inner dimension of the flow channels of the flow matrix. This is not found persuasive because Brown et al specifically teaches that the average diameter of the particles is less than the average pore size of the matrix (abstract) and as stated in the previous office actions the optimum dimension and diameter of the flow channels and particles size can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Therefore, it is the Examiner position that the combination of Brown et al with Charlton et al and Batz et al is appropriate and thus reads on the instantly recited claims.

Appellant argues that claims 47 and 68 are independently patentable. Appellant argues that claims 47 and 68 specify that the hydrophilic groups are hydroxy and that Batz et al teach epoxide groups. Appellant argues that Batz et al does not teach that the hydrophilic groups are hydroxy, carboxy, amino or sulphonate groups. This is not found persuasive because Batz et al specifically teaches hydroxyl (hydroxy) groups (col 13, lines 5-8).

Appellant argues that Bennich et al does not teach or suggest the use of a flow matrix as required by the present claims and that the method of Bennich et al involves contacting particles with a sample in solution. This is not found persuasive because Examiner has not relied upon Bennich et al for teaching flow matrices but rather has relied upon Charlton et al for teaching this limitation. Examiner has relied upon Bennich et al for immobilization of allergens used in assay and has relied upon the advantages of using these allergens. Further, Charlton et al discloses that the test cell can be used to detect any ligand which has been assayed using known immunoassay procedures or known to be detectable by such procedures.

Appellant argues that the methods and test kits defined by claims 48, 50, 54, 55, 69, 71, 75 and 76 are nonobvious over and patentably distinguishable from the combination of Charlton et al, Batz et al, brown et al and Devlin et al. Appellant argues that Devlin et al does not teach or suggest a method or test kit as presently claimed or for modifying the teachings of Charlton et al to provide such a method or test kit. Particularly, Appellants find not teaching or suggestion by Devlin et al for a method or test kit employing a flow matrix as presently claimed wherein an analytically detectable reactant (Reactant*) has labeled particles as an analytically detectable group and a biospecific affinity reactant (Capturer) is anchored to the flow matrix via immobilized particles of a size and function as claimed and exhibiting hydrophilic groups on their surface. This is not found persuasive because Examiner has not relied upon Devlin et al for these limitations but rather has relied upon Charlton, Batz and Brown for these limitations. Examiner has relied upon Devlin for teaching immunoassay procedures for

determining an analyte of interest. Furthermore, Charlton et al disclose that the test cell can be used to detect any ligand which has been assayed using known immunoassay procedures, or know to be detectable by such procedures.

Appellant argues that the deficiencies of Charlton et al in view of Batz et al and Brown et al with respect to the subject matter of claims 49, 59, 70 and 79 are not resolved by Dafforn et al. Appellant argues that Dafforn does not teach or suggest a method or test kit employing, in combination, an analytically detectable reactant (Reactant*) having labeled particles as an analytically detectable group and a Capturer which is anchored to the matrix by immobilized particles as defined and exhibiting hydrophilic groups on their surface This is not found persuasive because Examiner has not relied upon the Dafforn et al reference for these limitations. The above limitations are taught by the combination of Charlton et al in view of Batz et al and Brown et al. Examiner has relied upon Dafforn for the application of reagents upstream of a sample applicant and the advantages of this type of application.

Appellant argues a new argument that with respect to claims 49 and 70, Appellants find no teaching by Dafforn et al relating to a method which specifically determines an analyte which is an antibody of IgG, IgM or IgA type with specificity to autoantigens. This is not found persuasive because as stated in the previous office actions and above Dafforn teaches the detection of autoantibodies. Dafforn teaches that the analyte is the compound or composition to be measured that is capable of binding specifically to a ligand or receptor (col 4, lines27-31. Dafforn further teaches

that the receptor can be IgA, IgG, IgE and IgM. Therefore, Dafforn reads on the instantly recited claims.

Appellant argues that Dafforn et al fails to teach the limitations of claims 58 and 79 that the Reactant* is predeposited in the matrix upstream of a sample application site. This is not found persuasive because Dafforn et al teaches the device comprises a first means(20) for introducing a sample into the device and second means (22) other than the first means for introducing a liquid reagent other than the sample into the device (col 13, lines 32-44). Dafforn et al disclose that the liquid reagent can be an ancillary reagent such as a buffer or a labeled reagent (Reactant*). Dafforn et al disclose that the labeled reagent can be provided as liquid reagent or predeposited (col 19, line 15 – col 20, line 22). Therefore, Dafforn teaches the reactant* predeposited in the matrix upstream of sample application.

Appellant argues that the combination of Charlton et al, Batz et al, brown et al and Self does not render the presently claimed methods and kits obvious. Appellant argues that Self discloses an immunoassay using an amplified cyclic detection system and that the combination of Charlton et al, Batz et al, Brown et al and Self does not enable one of ordinary skill in the art to conduct the presently claimed methods or to made and use the presently claimed test kits. This is not found persuasive because as stated in the previous office action and above Self et al show that immunoassays are used for the detection and/or determination of autoimmune diseases and that and that immunoassays have a wide application, in both clinical and non-clinical fields and that they are particularly useful in any circumstance where it is necessary to detect and/or determine small or very small amounts of substances.

Furthermore, Charlton et al disclose that the test cell can be used to detect any ligand which has been assayed using known immunoassay procedures, or known to be detectable by such procedures.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Gary Counts
Examiner
Art Unit 1641
January 11, 2006

Conferees:

Long Le, SPE 1641

James Housel, SPE 1648